compositions with them; Emile Bisagni, et al., 514/287; 546/65, 196 [IMAGE AVAILABLE]

US PAT NO: 4,465,691 [IMAGE AVAILABLE] L8: 38 of 39

ABSTRACT:
Pyrido (3,4', 4,5) furo (3,2-g) coumarins or pyrido (3,4-h) psoralens having formula I ##STR1## wherein R is a hydrogen radical or a lower alkyl group having from 1 to 4 carbon atoms and R" is a methyl group or a methoxy group. These compounds are photobiologically active and are useful or medicinals and pharmaceutical compositions in association with ultraviolet radiation for treating skin diseases and as cosmetic compositions for skin pigmentation.

39. 4,464,354, Aug. 7, 1984, (3,4-c)-Pyrido psoralens, process of preparation, application in cosmetology and therapeutics, and cosmetological and pharmaceutical composition with them; Emile Bisagni, et al., 424/59; 514/287; 546/65, 221; 549/470 [IMAGE AVAILABLE]

US PAT NO: 4,464,354 [IMAGE AVAILABLE] L8: 39 of 39

ABSTRACT:
Monofunctional psoralen derivatives having the general formula ##STR1## wherein R represents a hydrogen atom, a lower alkyl group having from 1 to 4 atoms, preferably a methyl radical, or a lower alkoxy radical having from 1 to 4 carbon atoms, preferably a methoxy radical are described. The derivatives are photobiologically active and are useful in photochemical therapy and in cosmetics.

(FILE 'USPAT' ENTERED AT 13:19:29 ON 29 SEP 1999)
L1 383 S CHEE?/IN
L2 483 S BERNO, A?/IN OR YANG, R?/IN OR L1
L3 1689 S HUMAN AND MITOCHONDRIA? AND (RNA OR DNA OR NUCLEIC OR GE
NET
L4 56 S MITOCHONDRIA?(4A)MUTAT? OR MITOCHONDRIA?(4A)POLYMORPH?
L5 38 S L3 AND L4
L6 2 S L2 AND L5
L7 3 S L3 AND L2
L8 39 S L7 OR L5

08/856,376
APS
9-29-99
CIPK'D, AM

1. 5,925,520, Jul. 20, 1999, Multiplex sequencing method using primers of different lengths to detect polymorphisms; Gillian Tully, et al., 435/6, 91.1, 91.2; 536/24.33 [IMAGE AVAILABLE]

US PAT NO: 5,925,520 [IMAGE AVAILABLE] L8: 1 of 39

ABSTRACT:

A method is provided for determining the identity of at least two discrete single bases each adjacent to a predetermined nucleotide base sequence in a target sample having one or more types of polynucleotide chain. The method includes incorporating a capture group into the target sample and immobilizing the target sample by means of the capture group; mixing the target sample with (i) nucleotide primers which are complementary to predetermined base sequences such that they anneal to them at positions adjacent to the bases to be identified and (ii) at least two types of dideoxoy nucleoside triphosphate (ddNTPs), each type labelled with a distinguishable fluorescent group, and (iii) a nucleotide chain extending enzyme such that ddNTPs complementary to the bases to be identified are incorporated into the nucleotide primers; eluting the extending nucleotide primers, separating the types of extended nucleotide primer on basis of size or charge and identifying the ddNTPs incorporated into each type of nucleotide primer by reference to the fluorescent characteristics associated with the distinguishable groups. Primers and a test kit are provided for use in performance of the method.

2. 5,912,140, Jun. 15, 1999, Recombinant pneumocystis carinii aminoacyl tRNA synthetase genes, tester strains and assays; Susan K. Whoriskey, et al., 435/69.1, 69.7, 252.3, 254.2, 320.1; 530/350; 536/23.2, 23.4, 24.32 [IMAGE AVAILABLE]

US PAT NO: 5,912,140 [IMAGE AVAILABLE] L8: 2 of 39

ABSTRACT:

Recombinant **nucleic** acids which encode aminoacyl-tRNA sythetases of pneumocystis origin or portions of such enzymes, have been isolated. These **nucleic** acids can be used to make expression constructs and transformed host cells for the production of pneumocystis aminoacyl-tRNA synthetases. They can also be used in the further isolation of **nucleic** acids related by **DNA** sequence similarities, which also encode pneumocystis aminoacyl-tRNA synthetases, or portions thereof. A further embodiment of the invention is antisense **nucleic** acid which can hybridize to the **nucleic** acid which encodes the aminoacyl-tRNA

synthetase of pneumocystis. The invention also relates to enzymes, isolated and/or recombinant pneumocystis aminoacyl-tRNA synthetases. Antibodies which bind to these enzymes can be made and can be used in the purification and study of the enzymes. Tester strains, which are cells engineered to rely on the function of the tRNA synthetase encoded by an introduced cloned gene, can be used to test the effectiveness of drug candidates in the inhibition of the essential tRNA synthetase enzyme encoded by an introduced cloned pneumocystis gene.

3. 5,908,747, Jun. 1, 1999, Mutant gene causing a defect in **mitochondrial** recombination and a method for its detection; Takehiko Shibata, et al., 435/6, 320.1, 449; 536/23.5, 24.31 [IMAGE AVAILABLE]

US PAT NO: 5,908,747 [IMAGE AVAILABLE] L8: 3 of 39

ABSTRACT:
A multi-step method of detecting a gene in a nuclear chromosome which is involved in **mitochondrial** recombination is disclosed. The method disclosed includes the steps: a) fusing enucleated .omega..sup.- **mitochondrial** donor cells expressing a first marker gene with nucleus-containing .omega..sup.+ **mitochondrial** recipient cells expressing a second marker gene different from the first marker gene to form fused cells wherein the fused cells have one type of **mitochondria** and b) selecting fused cells that are .omega..sup.+ and express the first and second marker genes to identify those enucleated .omega..sup.- **mitochondrial** donor cells with a reduced recombination frequency. The method includes the further steps of judging that the gene in a nuclear chromosome of the recipient cells involved in **mitochondrial** recombination is normal when the **mitochondrial** recombination frequency is high or that the gene is mutated when the recombination frequency is low. The judging steps permit the detection of a mutant gene in a nuclear chromosome of the recipient cells used for cell fusion. An isolated mhr1 and MHR1 gene coding for a polypeptide is also disclosed.

4. 5,906,996, May 25, 1999, Tetramine treatment of neurological disorders; Michael A. Murphy, 514/674; 424/422; 514/654, 655 [IMAGE AVAILABLE]

US PAT NO: 5,906,996 [IMAGE AVAILABLE] L8: 4 of 39

ABSTRACT:
2,3,2 Tetramine (3,7-diazanonane-1,9-diamine) is propounded for the treatment of Parkinson's Disease and dementias characterized by **mitochondrial** damage in view of this compound's ability to completely

neutralize the dopainine-depriving effect of MPTP in laboratory animals up to 12 hours post MPTP injection, and to retain partial protection at suboptimal tissue levels for up to 36 hours. The effect of injecting combinations of MPTP and/or reducing agents and/or xenobiotics and/or depigmenting agents on Dopamine, Norepinephrine, Serotonin and Epinephrine levels demonstrated that MPTP and MPP+ act as reducing agents that mobilize copper and calcium, and sequester iron, and that the vulnerability of dopamine to these types of neurotoxins and to xenobiotics and metals can be corrected by administration of 2,3,2 tetramine that appears to redistribute metals between diverse storage pools and free metals in cytosol and regulate receptor mediated events, among other antidotal effects analogous to those of some of the endogenous polyamines.

5. 5,889,055, Mar. 30, 1999, L-carnitine and acetyl-L-carnitine combined for prevention and treatment of syndromes related to diseases of energy metabolism; James R. Howard, 514/561 [IMAGE AVAILABLE]

US PAT NO: 5,889,055 [IMAGE AVAILABLE] L8: 5 of 39

ABSTRACT:
A combination can be of L-carnitine and acetyl-L-carnitine administered orally or as parenteral injection in domesticated animals, especially pet animals, and humans for prevention or treatment of syndromes or diseases arising from dysfunctional energy metabolism. Syndromes involving skeletal and cardiac muscle benefited from L-carnitine, syndromes related to the central nervous system improved with acetyl-L-carnitine. Although the two cofactors do not substitute metabolically for each other effects of the combination are found to be synergistic.

6. 5,888,498, Mar. 30, 1999, Cellular and animal models for diseases associated with **mitochondrial** defects; Robert E. Davis, et al., 424/93.21, 93.3; 435/70.2, 366, 440, 441, 455, 467 [IMAGE AVAILABLE]

US PAT NO: 5,888,498 [IMAGE AVAILABLE] L8: 6 of 39

ABSTRACT:
Cybrid cell lines which have utility as model systems for the study of disorders that are associated with **mitochondrial** defects are described. The cybrids are constructed by treating immortal cell lines with an agent that irreversibly disables **mitochondrial** electron transport, and then transfecting the cells with **mitochondria** isolated from diseased tissue samples. Preferably, the immortal cell lines used are of an undifferentiated type that can be induced to differentiate, which results in the cybrids also being able to be induced to

differentiate. One such cybrid was constructed using neuroblastoma cells and **mitochondria** from a patient suffering from Alzheimer's Disease. Methods for using such cybrids for screening drugs and therapies for utility in treating such disorders are also provided. In addition, cybrid animals, methods of producing them, and methods of using them in drug and therapy screening are also provided.

7. 5,869,247, Feb. 9, 1999, Natural resistance associated macrophage protein and uses thereof; Charles Howard Barton, et al., 435/6, 91.2; 530/300, 387.1; 536/24.1, 24.31, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,869,247 [IMAGE AVAILABLE] L8: 7 of 39

ABSTRACT:

A natural resistance-associated macrophage protein and corresponding promoter and antibodies specific thereto are provided. The promoter region exhibits polymorphisms and is useful as a diagnostic agent.

8. 5,866,337, Feb. 2, 1999, Method to detect mutations in a **nucleic** acid using a hybridization-ligation procedure; Eric A. Schon, 435/6, 5, 91.1, 91.2, 91.3; 536/23.1, 24.3, 24.31, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,866,337 [IMAGE AVAILABLE] L8: 8 of 39

ABSTRACT:
The present invention provides a method for detecting a mutation in a **nucleic** acid molecule which comprises contacting the **nucleic** acid molecule with a probe. The probe comprises two covalently linked **nucleic** acid segments under conditions such that the unlinked end of each segment of the probe is capable of hybridizing with the **nucleic** acid molecule. This mixture is then contacted with a ligase under conditions such that the two hybridized probe segments will ligate and bind the **nucleic** acid molecule if the **nucleic** acid molecule contains the mutation. One would then determine the presence of bound **nucleic** acid molecule(s) and thereby detect the mutation in the **nucleic** acid molecule.

9. 5,861,242, Jan. 19, 1999, Array of **nucleic** acid probes on biological chips for diagnosis of HIV and methods of using the same; **Mark Chee**, et al., 435/5; 422/50, 68.1; 435/6, 283.1, 810; 436/501; 536/23.1, 24.1, 24.3, 24.31, 24.32, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,861,242 [IMAGE AVAILABLE] L8: 9 of 39

ABSTRACT:
The invention provides an array of oligonucleotide probes immobilized on a solid support for analysis of a target sequence from a **human** immunodeficiency virus. The array comprises at least four sets of oligonucleotide probes 9 to 21 nucleotides in length. A first probe set has a probe corresponding to each nucleotide in a reference sequence from a **human** immunodeficiency virus. A probe is related to its corresponding nucleotide by being exactly complementary to a subsequence of the reference sequence that includes the corresponding nucleotide. Thus, each probe has a position, designated an interrogation position, that is occupied by a complementary nucleotide to the corresponding nucleotide. The three additional probe sets each have a corresponding probe for each probe in the first probe set. Thus, for each nucleotide in the reference sequence, there are four corresponding probes, one from each of the probe sets. The three corresponding probes in the three additional probe sets are identical to the corresponding probe from the first probe or a subsequence thereof that includes the interrogation position, except that the interrogation position is occupied by a different nucleotide in each of the four corresponding probes.

10. 5,856,104, Jan. 5, 1999, Polymorphisms in the glucose-6 phosphate dehydrogenase locus; **Mark Chee**, et al., 435/6, 91.1, 91.2; 536/23.5, 24.31, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,856,104 [IMAGE AVAILABLE] L8: 10 of 39

ABSTRACT:
The invention provides **nucleic** acid segments of the glucose-6 phosphate dehydrogenase locus of the **human** genome including polymorphic sites. Allele-specific primers and probes hybridizing to regions flanking these sites are also provided. The **nucleic** acids, primers and probes are used in applications such as forensics, paternity testing, medicine and **genetic** analysis.

11. 5,853,742, Dec. 29, 1998, Cosmetic compositions containing lactate dehydrogenase inhibitors; John Brian Bartolone, et al., 424/401; 514/557 [IMAGE AVAILABLE]

US PAT NO: 5,853,742 [IMAGE AVAILABLE] L8: 11 of 39

ABSTRACT:
Inhibitors of lactate dehydrogenase stimulate keratinocyte proliferation and collagen synthesis in cutaneous tissues. The inhibitors are used preferably with certain co-active ingredients such as pyruvic acid, acetic acid, acetoacetic acid, .beta.-hydroxybutyric acid, a Krebs cycle

pathway metabolite, an aliphatic saturated or an unsaturated fatty acid containing from 8 to 26 carbon atoms, an .omega.-hydroxy acid containing from 22 to 34 carbon atoms, glutamic acid, glutamine, valine, alanine, leucine, and mixtures thereof.

12. 5,840,493, Nov. 24, 1998, **Mitochondrial** **DNA** **mutations** that segregate with late onset diabetes mellitus; Robert E. Davis, et al., 435/6, 91.2, 91.5; 536/24.31, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,840,493 [IMAGE AVAILABLE] L8: 12 of 39

ABSTRACT:
The present invention relates to **genetic** **mutations** in **mitochondrial** genes that segregate with diabetes mellitus. The invention provides methods for detecting such mutations, as a diagnostic for diabetes mellitus, either before or after the onset on clinical symptoms. Examples of specific **mutations** in the **mitochondrial** ATP synthase 8/6 gene and tRNA lysine gene are given. The invention also provides treatments for dysfunctions due to **mitochondrial** genes that segregate with diabetes mellitus. Cybrid cell lines are described which are useful as model systems for the study of the **mitochondrial** metabolic disorders that are associated with diabetes mellitus, and for identifying therapeutic compounds and treatments for this disease.

13. 5,837,832, Nov. 17, 1998, Arrays of **nucleic** acid probes on biological chips; **Mark Chee**, et al., 536/22.1; 422/68.1; 435/6, 91.1; 436/501; 536/23.1, 24.1, 24.3, 24.31, 24.32, 24.33, 25.3 [IMAGE AVAILABLE]

US PAT NO: 5,837,832 [IMAGE AVAILABLE] L8: 13 of 39

ABSTRACT:
DNA chips containing arrays of oligonucleotide probes can be used to determine whether a target **nucleic** acid has a nucleotide sequence identical to or different from a specific reference sequence. The array of probes comprises probes exactly complementary to the reference sequence, as well as probes that differ by one or more bases from the exactly complementary probes.

14. 5,827,702, Oct. 27, 1998, Ocular gene therapy; R. Andrew Cuthbertson, 514/44; 435/320.1, 455, 486 [IMAGE AVAILABLE]

US PAT NO: 5,827,702 [IMAGE AVAILABLE] L8: 14 of 39

ABSTRACT:

The invention relates to methods of ocular gene therapy.

15. 5,808,034, Sep. 15, 1998, Plant gene construct comprising male flower specific promoters; Ian George Bridges, et al., 536/24.1; 47/DIG.1; 536/23.5, 23.6, 23.7 [IMAGE AVAILABLE]

US PAT NO: 5,808,034 [IMAGE AVAILABLE] L8: 15 of 39

ABSTRACT:
Male sterility is imparted to a plant by a cascade of gene sequences which expresses a protein which disrupts the biosynthesis of viable pollen. Expression of the disrupter protein is restricted to male parts of the plant by an upstream promoter sequence which is specific to male flowers, the male specific promoter being under control of an operator sequence. The cascade also includes a gene encoding a repressor protein specific for that operator. Expression of the repressor protein is under control of a chemically inducible promoter which is inducible by the application to the plant by, spraying or like process, of an exogenous chemical. In the absence of the exogenous chemical inducer, no repressor protein is expressed, resulting in expression of the disrupter protein and, consequently, male sterility. Fertility may be restored to the plant, when required for maintenance of the line, by spraying with the inducer, resulting in expression of the repressor which binds the operator and inhibits expression of the disrupter protein.

16. 5,780,272, Jul. 14, 1998, Intron-mediated recombinant techniques and reagents; Kevin A. Jarrell, 435/91.31, 91.3, 91.32, 91.5; 536/23.1, 23.5, 23.53, 24.2 [IMAGE AVAILABLE]

US PAT NO: 5,780,272 [IMAGE AVAILABLE] L8: 16 of 39

ABSTRACT:
The present invention makes available methods and reagents for novel manipulation of **nucleic** acids. As described herein, the present invention makes use of the ability of intronic sequences, such as derived from group I, group II, or nuclear pre-mRNA introns, to mediate specific cleavage and ligation of discontinuous **nucleic** acid molecules. For example, novel genes and gene products can be generated by admixing **nucleic** acid constructs which comprise exon **nucleic** acid sequences flanked by intron sequences that can direct trans-splicing of the exon sequences to each other. The flanking intronic sequences can, by intermolecular complementation, form a reactive complex which promotes the transesterification reactions necessary to cause the ligation of discontinuous **nucleic** acid sequences to one another, and thereby generate a recombinant gene comprising the ligated exons.

17. 5,760,205, Jun. 2, 1998, Isolated nucleotide sequences corresponding to **mitochondrial** cytochrome oxidase genes; W. Davis Parker, et al., 536/23.5; 435/6; 536/24.31, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,760,205 [IMAGE AVAILABLE] L8: 17 of 39

ABSTRACT:
The present invention relates to **genetic** **mutations** in **mitochondrial** cytochrome oxidase genes that segregate with Alzheimer's disease (AD). The invention provides methods for detecting such mutations, as a diagnostic for Alzheimer's Disease, either before or after the onset of clinical symptoms. The invention further provides treatment of cytochrome oxidase dysfunction.

18. 5,712,259, Jan. 27, 1998, NADH and NADPH pharmaceuticals for treating chronic fatigue syndrome; Joerg G. D. Birkmayer, 514/52, 45, 46, 47; 536/26.13, 26.23, 26.24 [IMAGE AVAILABLE]

US PAT NO: 5,712,259 [IMAGE AVAILABLE] L8: 18 of 39

ABSTRACT:
A method for treating Chronic Fatigue Syndrome or alleviating symptoms thereof wherein the reduced form of nicotinamide adenine dinucleotide (NADH) or the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) or physiologically compatible salts or derivatives of NADH and/or NADPH are administered to a person suffering from the syndrome or its symptoms. Patients so treated exhibit greatly improved physical strength and performance over time, and their symptoms including fatigue, muscle pain and weakness, and headaches are greatly alleviated.

19. 5,690,944, Nov. 25, 1997, Cosmetic compositions containing lactate dehydrogenase inhibitors; John Brian Bartolone, et al., 424/401; 514/784 [IMAGE AVAILABLE]

US PAT NO: 5,690,944 [IMAGE AVAILABLE] L8: 19 of 39

ABSTRACT:
Inhibitors of lactate dehydrogenase stimulate keratinocyte proliferation and collagen synthesis in cutaneous tissues. The inhibitors are used preferably with certain co-active ingredients such as pyruvic acid, acetic acid, acetoacetic acid, .beta.-hydroxybutyric acid, a Krebs cycle pathway metabolite, an aliphatic saturated or an unsaturated fatty acid containing from 8 to 26 carbon atoms, an .omega.-hydroxy acid containing from 22 to 34 carbon atoms, glutamic acid, glutamine, valine, alanine,

leucine, and mixtures thereof.

20. 5,679,566, Oct. 21, 1997, Yeast NMD2 gene; Feng He, et al., 435/69.9, 252.3, 254.2, 325; 536/23.1, 23.7 [IMAGE AVAILABLE]

US PAT NO: 5,679,566 [IMAGE AVAILABLE] L8: 20 of 39

ABSTRACT:
The invention relates to the discovery of a gene, NMD2, named after its role in the Nonsense-Mediated mRNA Decay pathway, and the protein, Nmd2p, encoded by the NMD2 gene. The amino acid sequence of Nmd2p and the nucleotide sequence of the NMD2 gene encoding it are disclosed. Nmd2p is shown herein to bind to another protein in the decay pathway, Upf1p. A C-terminal fragment of the protein is also shown to bind Upf1p and, when overexpressed in the host cell, the fragment inhibits the function of Upf1p, thereby inhibiting the nonsense-mediated mRNA decay pathway. The invention also relates to methods of inhibiting the nonsense-mediated mRNA decay pathway to stabilize mRNA transcripts containing a nonsense codon which normally would cause an increase in the transcript decay rate. Such stabilization of a transcript is useful for the production of a recombinant protein or fragment thereof.

21. 5,670,320, Sep. 23, 1997, Detection of **mitochondrial** **DNA** **mutation** 14459 associated with dystonia and/or Leber's hereditary optic neuropathy; Douglas C. Wallace, et al., 435/6, 7.1, 7.2, 91.2; 536/24.3, 24.31, 24.32, 26.6 [IMAGE AVAILABLE]

US PAT NO: 5,670,320 [IMAGE AVAILABLE] L8: 21 of 39

ABSTRACT:
The present invention provides an assay for diagnosing or predicting a predisposition to dystonia and/or Leber's Hereditary Optic Neuropathy by detecting the presence of a **mutation** in **mitochondrial** **DNA**, in the oxidative phosphorylation (OXPHOS) gene ND6, that causes a substitution in amino acid 72 of the ND6 polypeptide. In particular, the mutation can be at mtDNA position 14459. Also provided are therapeutic treatments for dystonia and/or Leber's Hereditary Optic Neuropathy, as well as methods of screening compounds for effectiveness in treating these diseases and an animal model.

22. 5,604,099, Feb. 18, 1997, Process for detecting specific nucleotide variations and **genetic** polymorphisms present in **nucleic** acids; Henry A. Erlich, et al., 435/6, 91.2, 91.21, 194; 536/24.3, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,604,099 [IMAGE AVAILABLE] L8: 22 of 39

ABSTRACT:
Single or multiple nucleotide variations in **nucleic** acid sequence can be detected in **nucleic** acids by a process whereby the sample suspected of containing the relevant **nucleic** acid is repeatedly treated with primers, nucleotide triphosphates, and an agent for polymerization of the triphosphates and then denatured, in a process which amplifies the sequence containing the nucleotide variation if it is present. In one embodiment, the sample is spotted on a membrane and treated with a labeled sequence-specific oligonucleotide probe. Hybridization of the probe to the sample is detected by the label on the probe.

23. 5,595,730, Jan. 21, 1997, Lactate dehydrogenase inhibitors in cosmetic compositions; John B. Bartolone, et al., 424/70.1; 514/557, 574, 880 [IMAGE AVAILABLE]

US PAT NO: 5,595,730 [IMAGE AVAILABLE] L8: 23 of 39

ABSTRACT:
Certain combinations of lactate dehydrogenase inhibitors and specific carboxylic acids stimulate keratinocyte proliferation and collagen synthesis in skin.

24. 5,569,754, Oct. 29, 1996, **RNA** import elements for transport into **mitochondria**; R. Sanders Williams, et al., 536/23.5; 435/320.1 [IMAGE AVAILABLE]

US PAT NO: 5,569,754 [IMAGE AVAILABLE] L8: 24 of 39

ABSTRACT:
The invention relates to small RNAs encoded within the nucleus of mammalian cells that specifically import to the **mitochondria**. The RNAs bind to several nucleolar peptides and thus provide potential carriers for import of biological molecules, including metabolites and proteins, into the **mitochondrial** compartment. **Mitochondrial** dysfunction in several maternally inherited **human** diseases may be correctable employing linkage of **mitochondrial** import signal to **mitochondrial** tRNA sequences expressed from nuclear trans-genes without requirement for direct **genetic** transformation of **mitochondria**.

25. 5,565,323, Oct. 15, 1996, Cytochrome oxidase mutations aiding diagnosis of sporadic alzheimer's disease; W. Davis Parker, et al.,

435/6, 91.1, 91.2, 91.52; 536/23.5, 24.31 [IMAGE AVAILABLE]

US PAT NO: 5,565,323 [IMAGE AVAILABLE] L8: 25 of 39

ABSTRACT:
The present invention relates to **genetic** **mutations** in **mitochondrial** cytochrome oxidase genes that segregate with Alzheimer's disease (AD). The invention provides methods for detecting such mutations, as a diagnostic for Alzheimer's Disease, either before or after the onset clinical symptoms. The invention further provides treatment of cytochrome oxidase dysfunction.

26. 5,506,101, Apr. 9, 1996, Method for detection of susceptibility mutations for ototoxic deafness; Nathan Fischel-Ghodsian, et al., 435/6, 91.2; 536/24.31 [IMAGE AVAILABLE]

US PAT NO: 5,506,101 [IMAGE AVAILABLE] L8: 26 of 39

ABSTRACT:
Method for detection of **mitochondrial** nucleotide associated with predisposition for ototoxic deafness, especially deafness associated with the administration of aminoglycosides, is described.

27. 5,498,531, Mar. 12, 1996, Intron-mediated recombinant techniques and reagents; Kevin A. Jarrell, 435/91.31, 91.3, 91.32, 91.5; 536/23.1, 23.5, 23.53 [IMAGE AVAILABLE]

US PAT NO: 5,498,531 [IMAGE AVAILABLE] L8: 27 of 39

ABSTRACT:
The present invention makes available methods and reagents for novel manipulation of **nucleic** acids. As described herein, the present invention makes use of the ability of intronic sequences, such as derived from group I, group II, or nuclear pre-mRNA introns, to mediate specific cleavage and ligation of discontinuous **nucleic** acid molecules. For example, novel genes and gene products can be generated by admixing **nucleic** acid constructs which comprise exon **nucleic** acid sequences flanked by intron sequences that can direct trans-splicing of the exon sequences to each other. The flanking intronic sequences can, by intermolecular complementation, form a reactive complex which promotes the transesterification reactions necessary to cause the ligation of discontinuous **nucleic** acid sequences to one another, and thereby generate a recombinant gene comprising the ligated exons.

28. 5,494,794, Feb. 27, 1996, Detection of **mitochondrial** **DNA**

mutations associated with Alzheimer's disease and Parkinson's disease; Douglas C. Wallace, 435/6, 91.2, 91.52 [IMAGE AVAILABLE]

US PAT NO: 5,494,794 [IMAGE AVAILABLE] L8: 28 of 39

ABSTRACT:
This invention provides a method of Alzheimer's disease and/or Parkinson's Disease. The method comprises detecting in a sample from a subject the presence of a mutation, for example, in nucleotide position 4,336, 3,397, 3,196 or an insertion between positions 956 and 965, of **mitochondrial** **DNA**. The presence of the mutation indicates the presence of or a predisposition to Alzheimer's and Parkinson's disease. Since each mutation increases the likelihood of developing or having Alzheimer's and Parkinson's disease, the detection of more than one of the mutations in an individual can increase the probability of having or developing the disease. The invention also provides a method of determining mutations associated with the presence of or predisposition to Alzheimer's and/or Parkinson's disease. The method comprises:
(a) obtaining a **mitochondrial** **DNA**-containing sample from a subject with Alzheimer's and Parkinson's disease;
(b) determining the presence of **mutations** in the **mitochondrial** **DNA**;
(c) comparing the mutations to mutations found in a normal subject; and
(d) determining which mutations have a greater rate of occurrence in the subject with Alzheimer's and Parkinson's disease.

29. 5,468,613, Nov. 21, 1995, Process for detecting specific nucleotide variations and **genetic** polymorphisms present in **nucleic** acids; Henry A. Erlich, et al., 435/6, 91.2, 91.21, 194; 536/24.3, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,468,613 [IMAGE AVAILABLE] L8: 29 of 39

ABSTRACT:
Single or multiple nucleotide variations in **nucleic** acid sequence can be detected in **nucleic** acids by a process whereby the sample suspected of containing the relevant **nucleic** acid is repeatedly treated with primers, nucleotide triphosphates, and an agent for polymerization of the triphosphates and then denatured, in a process which amplifies the sequence containing the nucleotide variation if it is present. In one embodiment, the sample is spotted on a membrane and treated with a labeled sequence-specific oligonucleotide probe. Hybridization of the probe to the sample is detected by the label on the probe.

30. 5,466,576, Nov. 14, 1995, Modulation of PIF-1-type helicases; Vincent P. Schulz, et al., 435/6, 183, 193 [IMAGE AVAILABLE]

US PAT NO: 5,466,576 [IMAGE AVAILABLE] L8: 30 of 39

ABSTRACT:
Method for affecting viability of a eucaryotic cell by contacting the cell with a modulator of the activity of a PIF-1-type helicase in the cell. Such contacting specifically increases or decreases the specific activity of the helicase in the cell.

31. 5,310,664, May 10, 1994, Site specific double stranded **DNA** endonuclease; Ronald A. Butow, et al., 435/91.53, 199 [IMAGE AVAILABLE]

US PAT NO: 5,310,664 [IMAGE AVAILABLE] L8: 31 of 39

ABSTRACT:
An endonuclease which cleaves double stranded **DNA** at a specific site, producing staggered ends with 4 base pair, 3' overhangs, has been isolated, purified and characterized. A method of producing sufficient quantities of the endonuclease for purification and characterization is disclosed. A method to use the endonuclease to cleave **DNA**, producing fragments useful for gene mapping is also disclosed.

32. 5,292,639, Mar. 8, 1994, Association of bovine **mitochondrial** **DNA** with traits of economic importance; Donald C. Beitz, et al., 435/6; 536/23.1, 24.3, 25.4 [IMAGE AVAILABLE]

US PAT NO: 5,292,639 [IMAGE AVAILABLE] L8: 32 of 39

ABSTRACT:
A method of genetically evaluating animals by using **mitochondrial** **DNA** is disclosed. **Polymorphisms** in **mitochondrial** **DNA** are detected by isolating, fragmenting, and sequencing the **DNA**. The restriction patterns and nucleotide sequences of **mitochondrial** **DNA** of different animals are correlated to expressed traits in the animals. This may be confirmed by comparing results to expression of the trait in maternal lineages of animals. Further, effects of maternal lineages are determined by partitioning maternal **genetic** variation from nuclear variation.

33. 5,198,337, Mar. 30, 1993, Assay for gene deletion of GST-1 in **human** samples based on the polymerase chain reaction; William D. Henner, et al., 435/6, 91.2; 436/501, 811; 536/24.33 [IMAGE AVAILABLE]

US PAT NO: 5,198,337 [IMAGE AVAILABLE] L8: 33 of 39

ABSTRACT:
Methods for the detection of GST-1 gene deletion in **human** blood or tissue samples. The polymerase chain reaction is used to identify the presence or absence of the GST-1 gene in **human** clinical samples as a means of assessing susceptibility to neoplasia or toxicity upon chemical exposure. The method may also be used on **human** tumor samples to assess the possibility of resistance to certain chemotherapeutic agents.

34. 5,198,336, Mar. 30, 1993, Bioassay for chemicals which generate prooxidant states; Lynda M. Knobeloch, et al., 435/4, 25, 26; 436/35, 164 [IMAGE AVAILABLE]

US PAT NO: 5,198,336 [IMAGE AVAILABLE] L8: 34 of 39

ABSTRACT:
A bioassay making use of submitochondrial particles to test for the presence of toxic substances which induce prooxidant states in vivo. The assay uses complex I of the electron transport enzymes on the submitochondrial particles which are capable of donating electrons to the toxicant in solution. The presence of any activated oxygen species in the assay solution is detected spectrophotometrically by the adrenochrome reaction.

35. 5,194,373, Mar. 16, 1993, Method of determining endothelial cell coverage of a prosthetic surface; Stuart K. Williams, et al., 435/34, 39 [IMAGE AVAILABLE]

US PAT NO: 5,194,373 [IMAGE AVAILABLE] L8: 35 of 39

ABSTRACT:
Determination of effectiveness of microvascular endothelial cell seeding upon a vascular graft surface within the operating room environment would be desirable to maintain quality control in any clinical trial. A number of fluorescent dyes including mithramycin, Hoechst 33342, sulfofluorescein diacetate, Nile Red, rhodamine 123, and PKH26-GL were evaluated for their ability to fluorescently label uncultured microvascular endothilial cells on graft material and subsequently allow determination of seeded cell number and cell spreading. Rhodamine 123 and PKH26-GL produced the most desirable characteristics. The selected non-toxic fluorescent dyes allowed excellent cell visualization after a 30 minute incubation. Unlike the other fluorescent dyes evaluated, the selected non-toxic fluorescent dyes caused the cellular cytoplasm to fluoresce bright orange at a 510 nm excitation wavelength while the

underlying polyethyleneterephthalate polyester or expanded polytetrafluorethylene demonstrated minimal autofluorescence. No inhibitory effect on cell attachment to plastic or subsequent cell growth in culture was observed. This technique is useful in the operating room to visualize part or all of an microvascular endothelial cell-seeded graft and to permit a quantitative as well as qualitative evaluation of the seeding process to enhance graft patency.

36. 5,185,244, Feb. 9, 1993, **Genetic** test for hereditary neuromuscular disease; Douglas C. Wallace, 435/6, 91.2; 436/63, 94, 501; 536/23.1, 24.31 [IMAGE AVAILABLE]

US PAT NO: 5,185,244 [IMAGE AVAILABLE] L8: 36 of 39

ABSTRACT:
The present invention relates a method and manufacture for detecting neuromuscular disease, particularly Leber's hereditary optic neuropathy, by ascertaining whether a point mutation has occurred at the 11778 nucleotide position in the **mitochondrial** **DNA** of a patient. The invention provides methods to detect this mutation including digestion of the patient's mtDNA with restriction endonucleases followed by analysis of the resulting fragments, differential hybridization of oligonucleotides procedures, and differential PCR techniques.

37. 4,965,188, Oct. 23, 1990, Process for amplifying, detecting, and/or cloning **nucleic** acid sequences using a thermostable enzyme; Kary B. Mullis, et al., 435/6, 69.1, 91.2, 91.41 [IMAGE AVAILABLE]

US PAT NO: 4,965,188 [IMAGE AVAILABLE] L8: 37 of 39

ABSTRACT:
A process for amplifying any target **nucleic** acid sequence contained in a **nucleic** acid or mixture thereof comprises treating separate complementary strands of the **nucleic** acid with a molar excess of two oligonucleotide primers and extending the primers with a thermostable enzyme to form complementary primer extension products which act as templates for synthesizing the desired **nucleic** acid sequence. The amplified sequence can be readily detected. The steps of the reaction can be repeated as often as desired and involve temperature cycling to effect hybridization, promotion of activity of the enzyme, and denaturation of the hybrids formed.

38. 4,465,691, Aug. 14, 1984, (3,4';4,5)-Pyrido (3,2-g)-furo coumarins or (3,4-h) pyrido psoralens process of preparation, applications in cosmetology and in therapeutics, and cosmetological and pharmaceutical